

UV Radiation: Risks and Protective Effects

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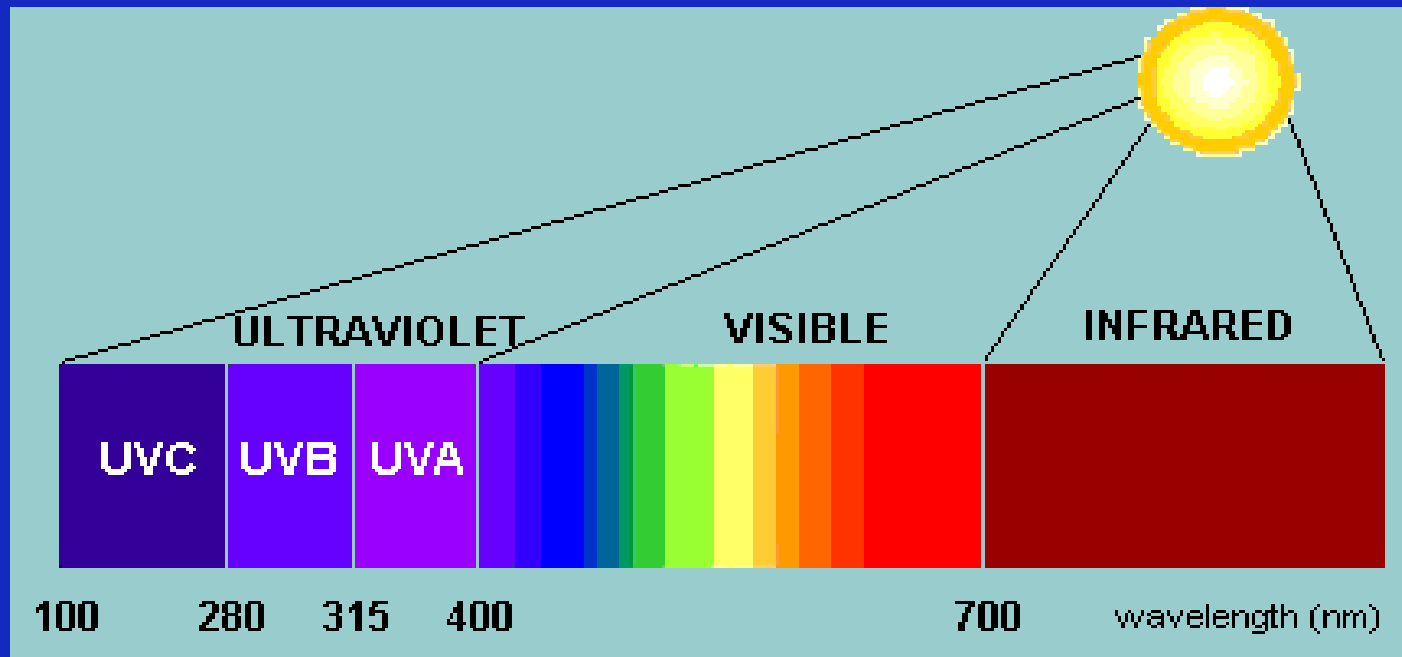
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Outline of Presentation

1. Background on Ultraviolet Radiation (UVR)
2. UVR: Risks
3. UVR: Role in Cancer Prevention?
4. Vitamin D: the Responsible Agent?
5. Policy Dilemma

Background on UV Radiation

Ultraviolet Radiation Spectrum

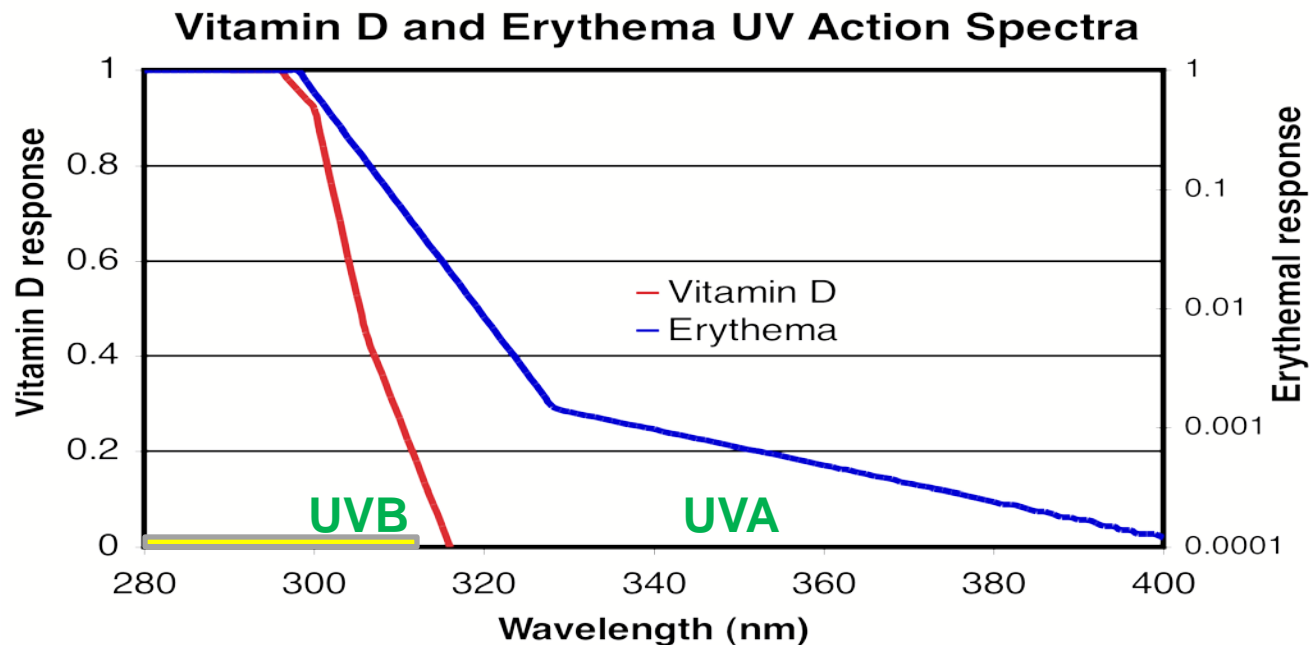


Terrestrial life dependent on radiant energy from the sun

~5% of solar radiation is **UVR**, which spans 100-400 nm

Three bands, **UVA**, **UVB**, and **UVC** based on wavelength and biological effect.

UVR: Biological Wavelengths



UVC: Completely absorbed by atmosphere

UVB: 90% absorbed by atmosphere

Source of vitamin D; key factor in DNA damage

UVA: 95% of what reaches the earth

Penetrates deeper in skin

Considered less damaging

UVR: The Risks

UVR: Adverse Health Effects

- Acute and chronic effects: skin, eye, and immune system
- Skin:
 - Acute - erythema (sunburn)
 - Chronic: degenerative changes in cells, fibrous tissue:
 - freckles, nevi
 - Loss of skin's elasticity (wrinkles and dry, coarse skin)



UV: Skin Cancer

- UVR is the major cause of skin cancers
- 50% of all U.S. cancers
- IARC determined that “there is sufficient evidence of solar radiation for cutaneous malignant melanoma and nonmelanocytic skin cancer.” (IARC, Solar and Ultraviolet Radiation Vol. 55)



Non-melanoma and melanoma skin cancers

- BCC and SCC— >1 million cases in 2007
 - 20% of Americans
 - 5th most costly cancer to Medicare
- Melanoma-
 - U.S. lifetime risk increased from 1/1500 in 1935 to 1/63 currently
 - 60,000 cases in 2007
 - 1st or 2nd most common cancer in U.S., ages 15-29 years



Cataracts

- Some evidence for role of UVR in 3 cataract types
- Strongest evidence for cortical cataract, affecting the cortex of the lens (WHO, Solar Ultraviolet Radiation (No. 13) 2006)
- World-wide: 16 million currently blind due to cataracts
 - Of these 20% estimated due to UVR (<http://www.who.int/mediacentre/factsheets/who271/en/>)

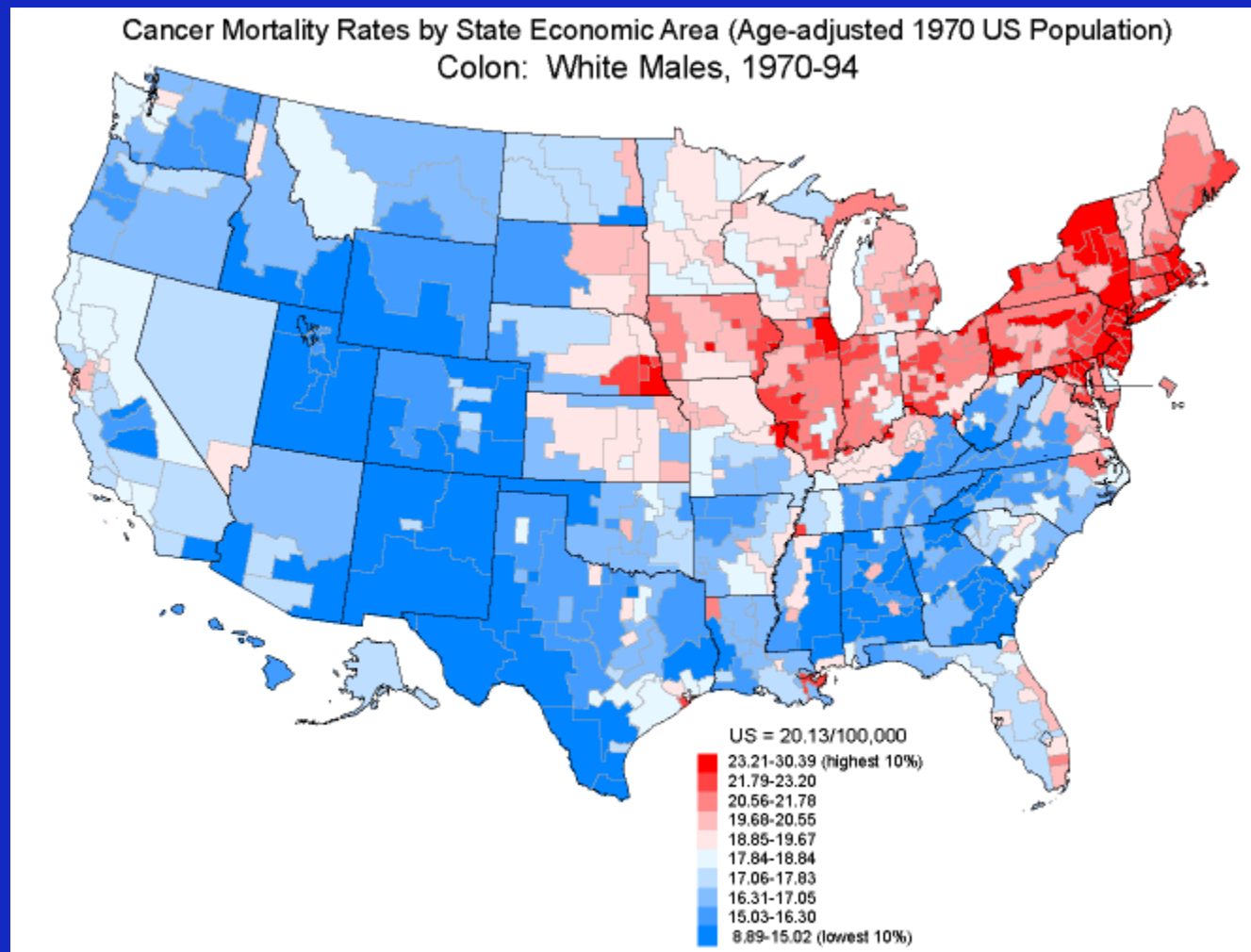
WHO Evaluates Global Burden

- WHO undertook a burden of disease analysis
- Concluded “globally, excessive solar UVR exposure caused the loss of approximately 1.5 million [disability adjusted life years] DALY’s ... and 60,000 premature deaths ”
- Greatest burden: melanoma, cataracts, and sunburn (WHO, Solar Ultraviolet Radiation (no.13) 2006)

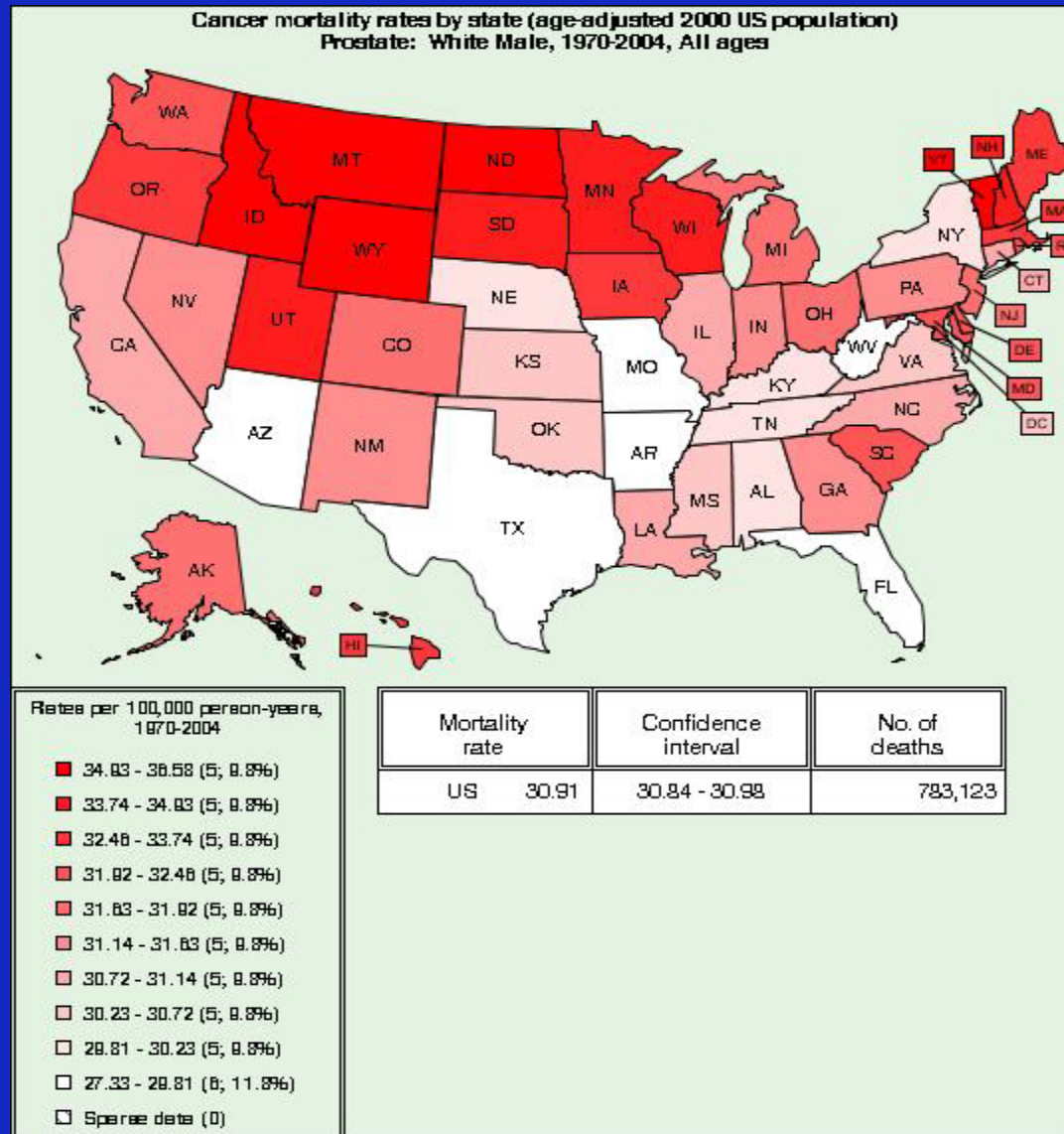
UVR : Health Benefits?

Focus on Cancer Prevention

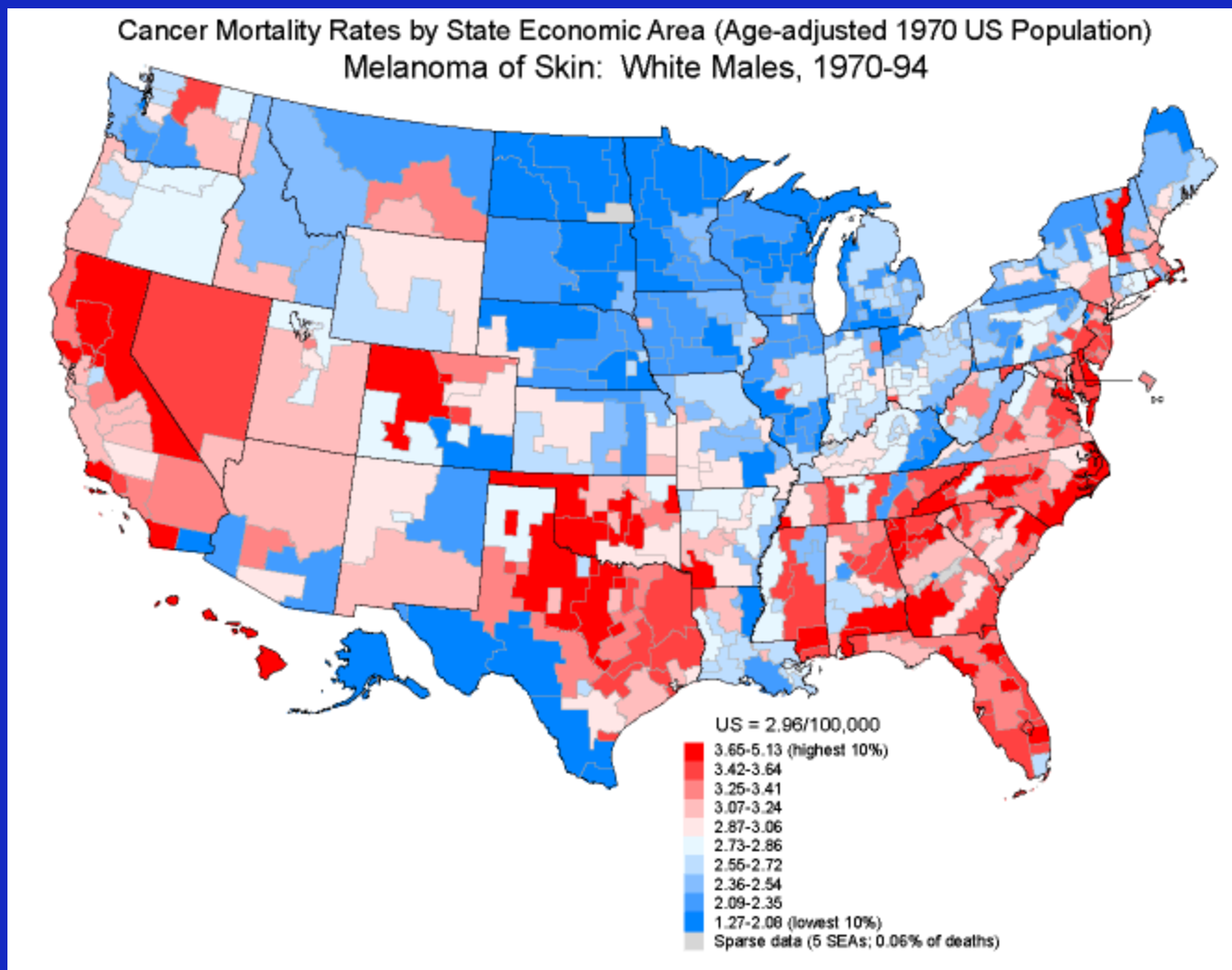
Colon Cancer Mortality



Prostate Cancer Mortality



Melanoma Mortality



Solar UV also inversely correlated with cancer mortality rates for:

- Breast cancer (Garland et al. Prev Med 1990;19:614-22)
- Ovarian cancer (Lefkowitz and Garland, IJE 1994;23:1133-6)
- Non-Hodgkin lymphoma (Hartge et al. JNCI 1996;88:298-300)

Some Background on Vitamin D, the Responsible Agent?

Sources of Vitamin D

- Directly related to dietary and cutaneous synthesis
- 70-100% of vitamin D from UV exposure

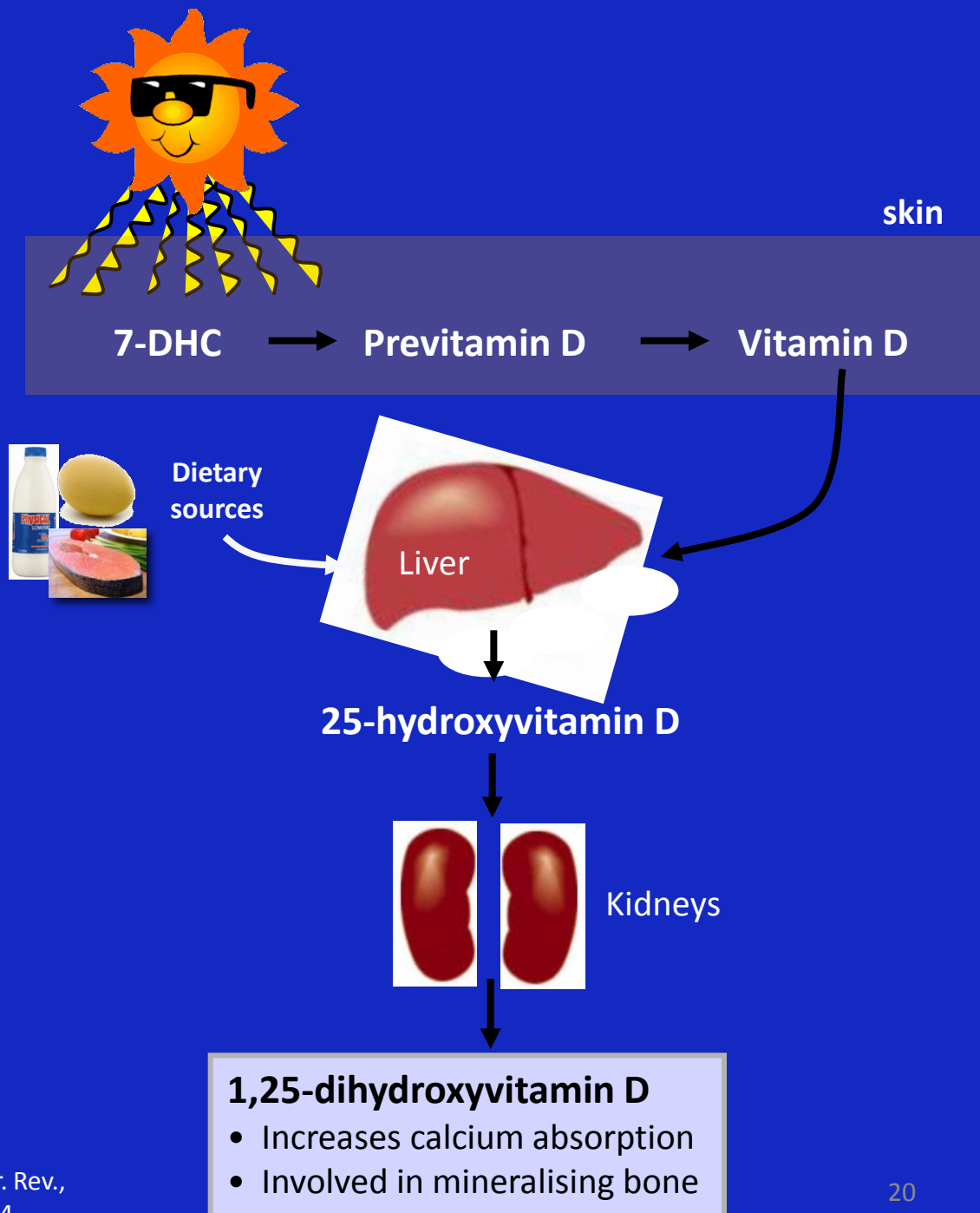


Vitamin D: Physiological Effects

1. Vitamin D is a hormone, not a vitamin
2. Regulates blood calcium levels
3. Necessary for bone development and bone health
4. Influences other pathways (e.g., immune system, other hormones)

Synthesis of Vitamin D by UV

1. 7-dehydrocholesterol in the skin absorbs UV to make **previtamin D**
2. Thermal reaction over several hours to make **Vitamin D**
3. Hydroxylation in liver makes **25-(OH)D**
4. Final hydroxylation in kidneys produces the active **1,25-(OH)₂D**



Vitamin D and Cancer

Experimental Evidence

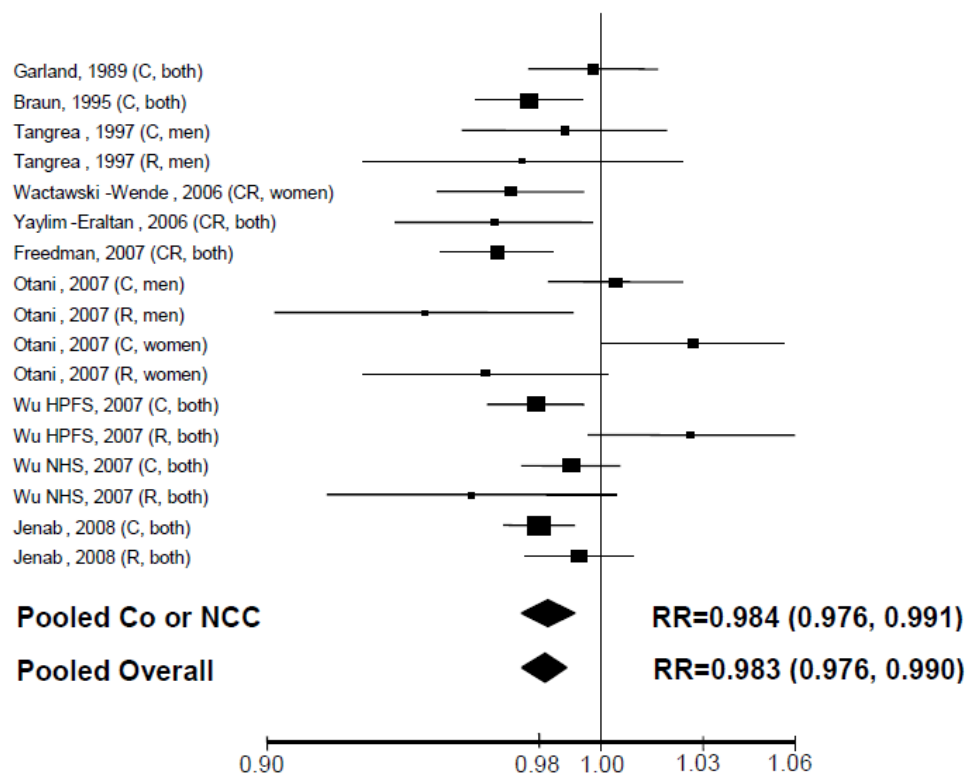
In vitro evidence:

1,25(OH)₂D

- induces differentiation
- inhibits proliferation
- inhibits invasiveness & angiogenesis in cell lines

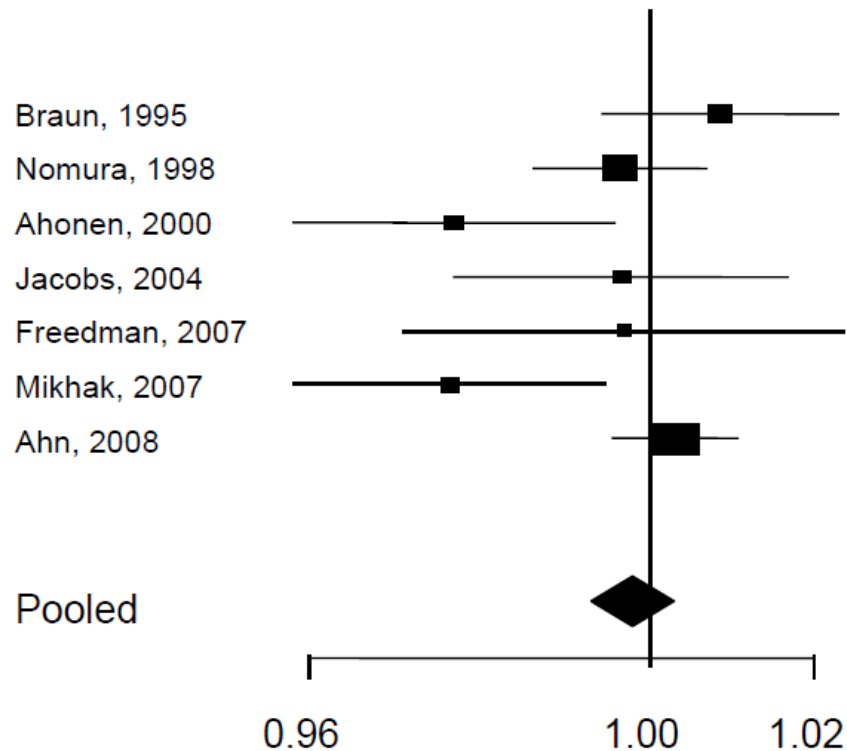
Observational Epidemiological Evidence: Colorectal Cancer

Figure 13.1 - Dose-response relative risks for colorectal cancer due to an increase of 1 unit of ng/mL serum level of 25-hydroxyvitamin D. The relative risk "pooled Co or NCC" is calculated after exclusion of case-control studies (C is colon, R is rectum, Co is cohort studies, NCC is nested case-control studies)



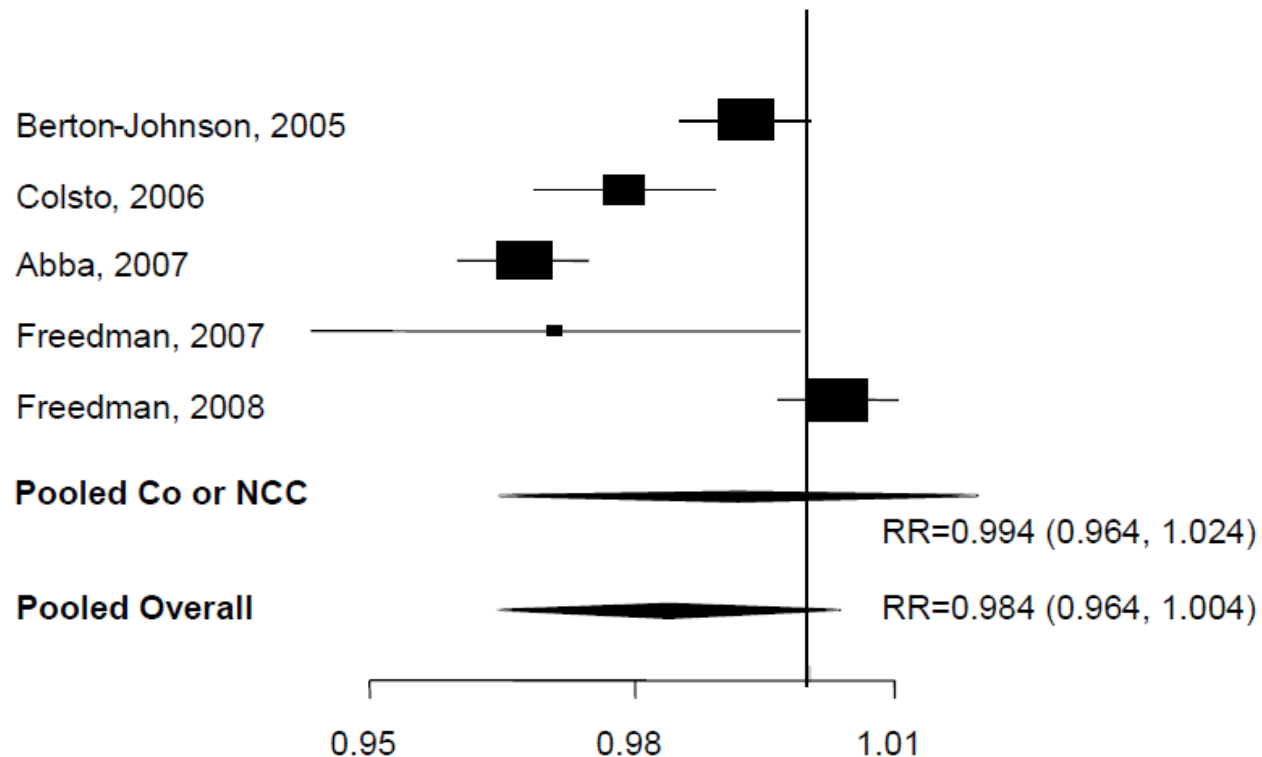
Prostate Cancer

Figure 13.5 - Dose-response relative risks between 25-hydroxyvitamin D and prostate cancer. All studies were cohort or nested-case control designs.



Breast Cancer

Figure 13.4 - Dose-response relative risks for breast cancer due to an increase of 1 unit of ng/mL serum level of 25-hydroxyvitamin D. All studies are on breast cancer incidence, but Freedman *et al.*, 2007, that used breast cancer mortality as endpoint. The relative risk "pooled Co or NCC" is calculated after exclusion of case-control studies (Co is cohort studies, NCC is nested case-control studies)

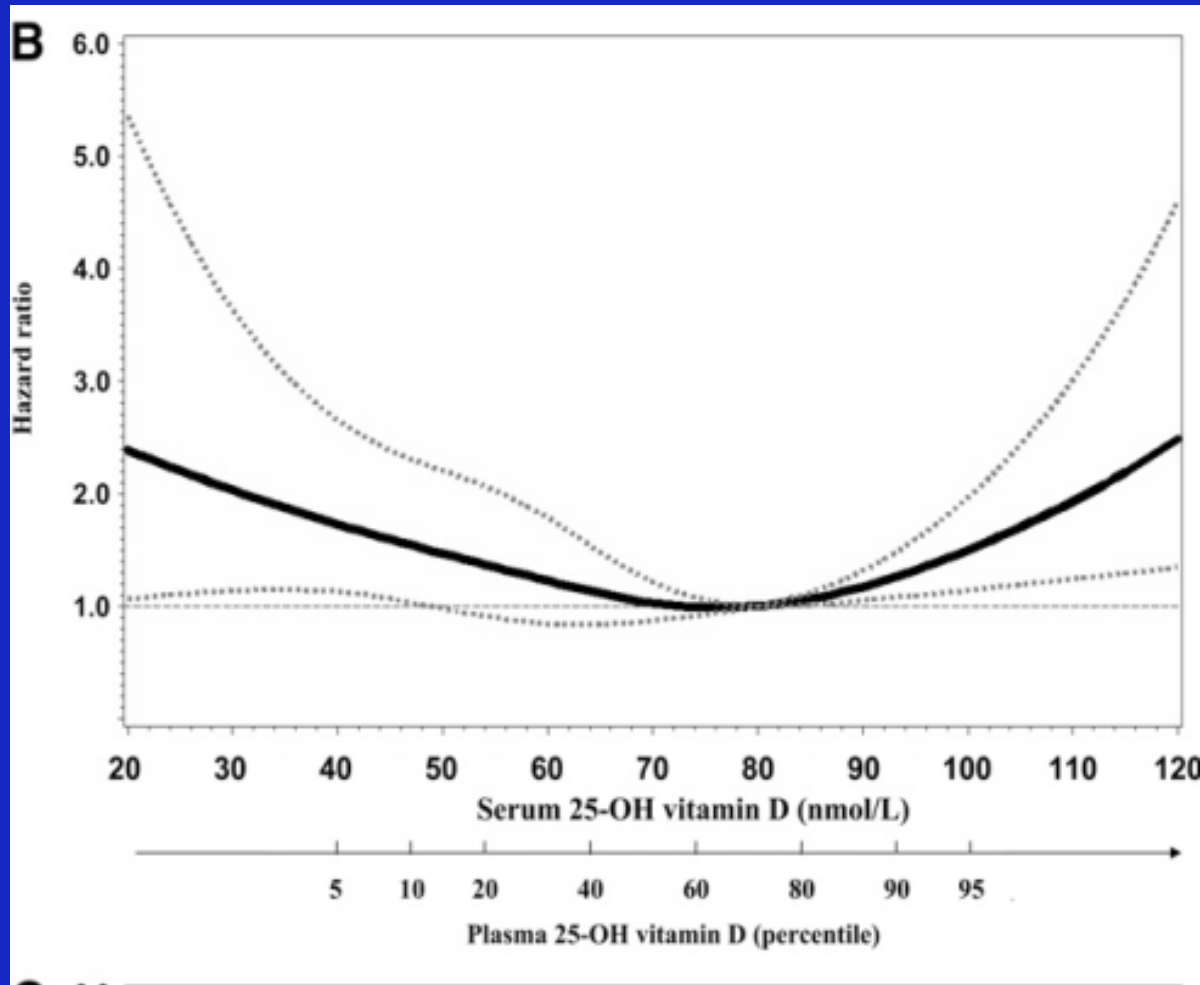


Pancreatic Cancer

Three studies found:

Elevated risks with increased levels of vitamin D
in Finnish male smokers (Solomon et al. Cancer Res 2006)
in northern areas of U.S. (Solomon et al. Cancer Res 2009)
in pooled analysis (U.S. and other countries)
(Solomon et al. Am J Epidemiol 2010)

Cancer Mortality in Men



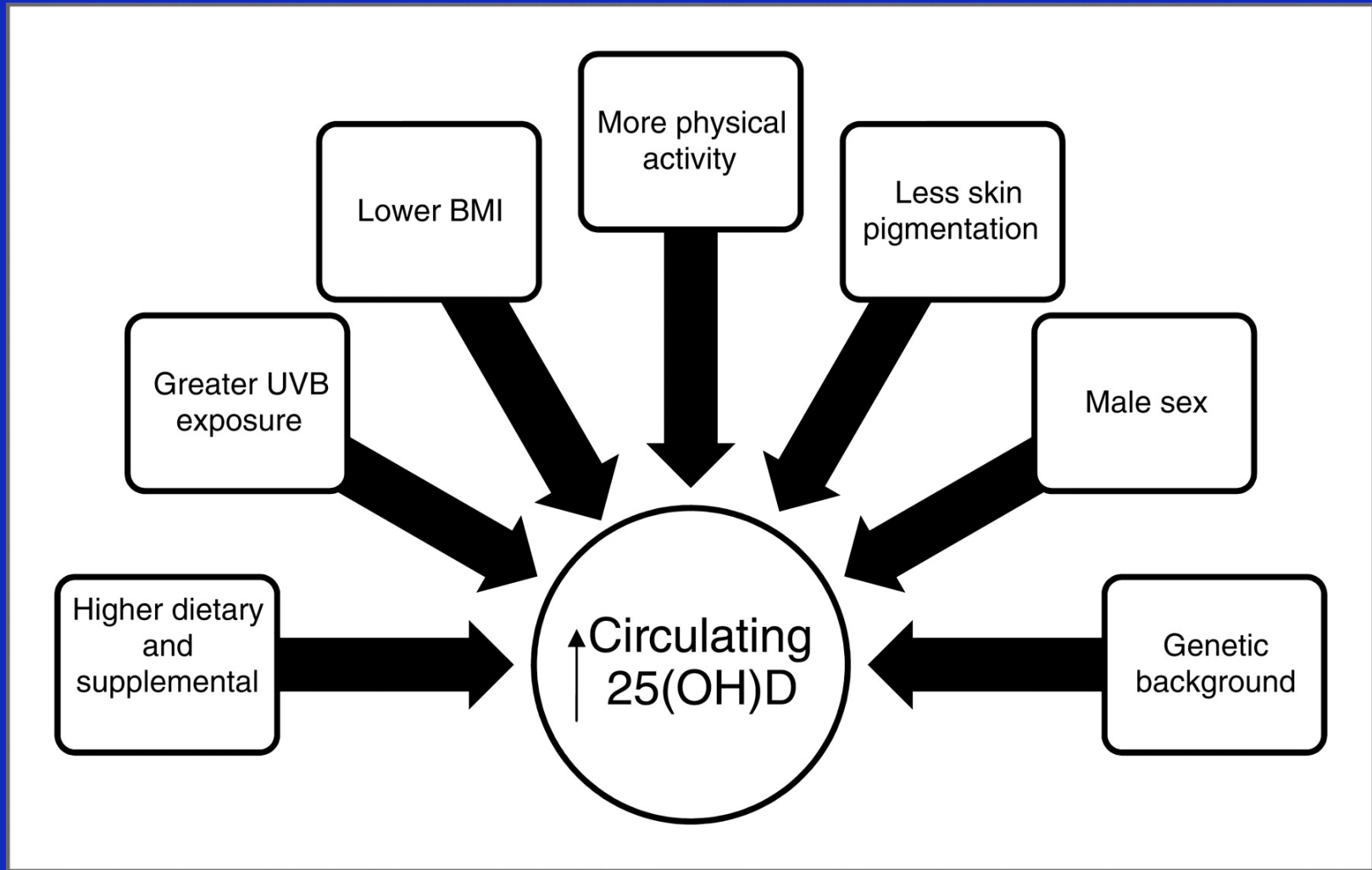
Summary of Observational Studies

- Mainly null results
- Best evidence of cancer **prevention** for colorectal cancer
- Some evidence of **adverse** associations (aggressive prostate cancer, pancreatic cancer, total cancer mortality in men)

Limitations of Observational Studies

- Single blood measurement
 - What if intra-individual measurements vary greatly?
- Confounding
 - Circulating vitamin D related to other factors that may be protective

Contributors to circulating concentrations of 25(OH)D.



Jacobs E T et al. Cancer Epidemiol Biomarkers Prev
2011;20:585-590

Institute of Medicine Reviewed Vitamin D and Health Outcomes (2010)

- Cancer
- Cardiovascular Disease
- Diabetes
- Falls
- Immune responses
(autoimmune diseases)
- Infectious diseases
- Autism
- Depression
- Physical performance
- Reproductive outcomes
- Skeletal Health

IOM Committee Concluded:

- Vitamin D and calcium play a key role in skeletal health
- “For extra-skeletal outcomes, including cancer, cardiovascular disease, diabetes, and autoimmune disorders, the evidence was inconsistent [and] inconclusive as to causality.”

Ross et al. J Clin Endocrin Metabl 2011.

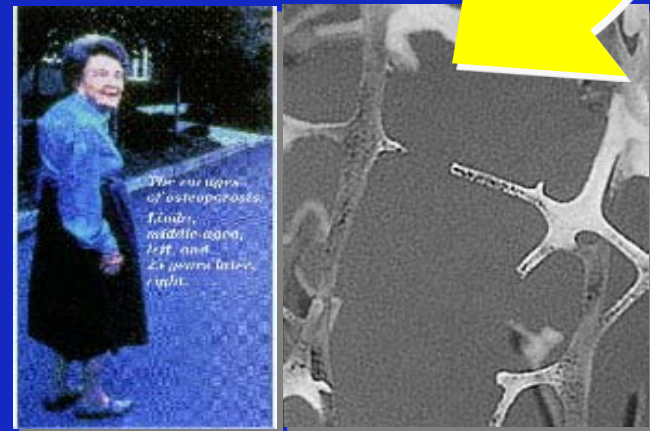
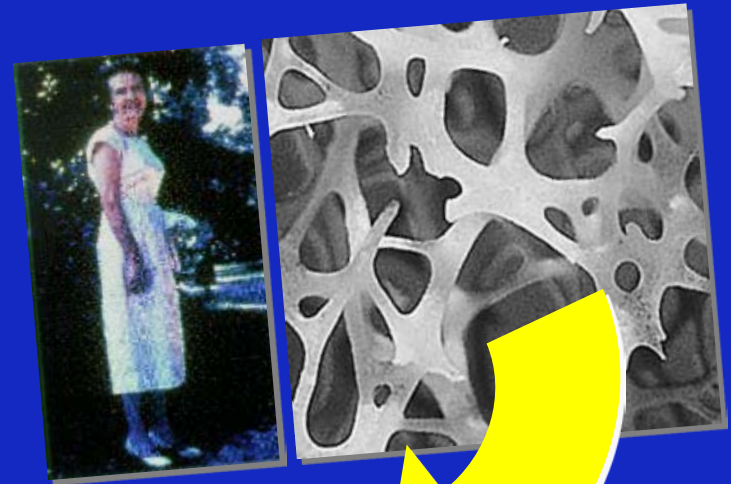
Inadequate Vitamin D : Bone Diseases

Contributes to **osteoporosis**¹

Likely protective effect against **falls**² and **fractures**³, especially when combined with calcium

Causes **rickets**⁴:
skeletal deformities in
children

Causes **osteomalacia**⁵: (adults)
bone pain, aches, muscle
weakness



1 Dawson-Hughes et al., 2005, Osteoporos Int 16(7) pp. 713-6.

2 Bischoff-Ferrari HA et al., 2004, JAMA 291 pp. 1999-2006.

3 Bischoff-Ferrari HA et al., 2009, Arch Intern Med 169(6) pp. 551-61.

Tang BM et al., 2007, Lancet 370(9588) pp. 657-66.

4 Pettifor JM, 2008, Indian J Med Res 127(3) pp. 245-9.

5 Holick, MF, 2007, NEJM 357(3) pp. 266-81.

A Policy Dilemma: What is the Public Health Message?



- Risks
 - Skin cancer
 - Skin aging
 - Cataracts
 - 0.1% of global burden of disease
 - Possible other risks



- Benefits
 - Bone health
 - Non-skin cancers?
 - Other diseases (e.g., autoimmune diseases)?

What Public Health Message Do We Promote?

- Increase sun exposure?
- Increase vitamin D supplementation and fortification?
- Both?

More Sun



- “Dr. Holick ... suggests that people allow their face, arms, and hands to be exposed for **5 to 15 minutes** two or three times per week.”

October 25, 2003 report from Holick seminar at Harvard SPH

- How would recommendations vary by location, season, pigmentation?
- How will the message be interpreted?

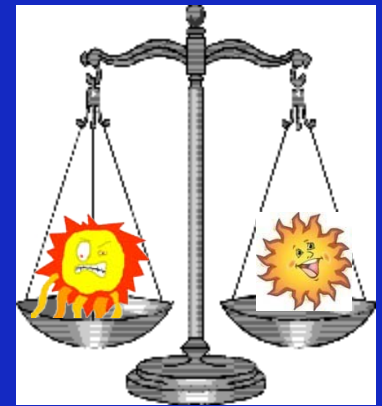
Increase Vitamin D Supplementation



“taking a vitamin D supplement all year long and using proper sun protection would appear to be the ideal strategy.” Lim, JAAD 2005;52:868-76 (Conclusion of an American Academy of Dermatology Association sponsored conference)

What is the appropriate supplement dose?

Some of Each



“To **minimize** the health risks associated with UVB radiation exposure while **maximizing** the potential benefits of optimum Vitamin D status, **supplementation and small amounts of sun exposure** are the preferred methods of obtaining vitamin D.” Conclusion of a conference sponsored by the Canadian Cancer Society

Conclusions

- To balance the risks and benefits of UVR, we need to know:
 - The full range of UVR risks
 - Does UVR/vitamin D protect against non-skin cancer, other diseases? Is it harmful for these outcomes?
 - Are these effects due to vitamin D?
 - At what levels does it protect or harm?
 - How do UVR and other exposures, including genes, contribute to vitamin D levels?

The End